Engineering antigen-specific T cells from genetically modified human hematopoietic stem cells in immunodeficient mice.

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Public Summary:

Scientific Abstract:
There is a desperate need for effective therapies to fight chronic viral infections. The immune response is normally fastidious at controlling the majority of viral infections and a therapeutic strategy aimed at reestablishing immune control represents a potentially powerful approach towards treating persistent viral infections. We examined the potential of genetically programming human hematopoietic stem cells to generate mature CD8+ cytotoxic T lymphocytes that express a molecularly cloned, "transgenic" human anti-HIV T cell receptor (TCR). Anti-HIV TCR transduction of human hematopoietic stem cells directed the maturation of a large population of polyfunctional, HIV-specific CD8+ cells capable of recognizing and killing viral antigen-presenting cells. Thus, through this proof-of-concept we propose that genetic engineering of human hematopoietic stem cells will allow the tailoring of effector T cell responses to fight HIV infection or other diseases that are characterized by the loss of immune control.